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High Production Volume (HPV) Challenge Program

Asphalt, sulfonated, sodium salt
CAS Number 68201-32-1
Test Plan

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ABBREVIATIONS

ACC = American Chemistry Council
API = American Petroleum Institute
BCF = predicted bioconcentration factor
bw = body weight
CPChem = Chevron Phillips Chemical Company LP
EC = Commission of the European Communities
HPV = High Production Volume
IUCLID = International Uniform Chemical Information Dataset
Koc = organic carbon partition coefficient
Kow = n-octanol/water partition coefficient
LC_{50} = lethal concentration (to 50% of animals dosed)
LD_{50} = lethal dose (to 50% of animals dosed)
LOAELs = lowest observed adverse effect levels
NOAELs = no observed adverse effect levels
OECD = Organisation for Economic Cooperation and Development
PAH = polycyclic aromatic hydrocarbons
PDII = primary dermal irritation index
Pow = n-octanol/water partition coefficient
ppm = parts per million
R = asphalt-based complex alkyl aromatic hydrocarbon mixture
SARA = Saturates, Aromatics, Resins, and Asphaltenes
SAS = Asphalt, Sulfonated, Sodium Salt
SIDS = Screening Information Data Set
USEPA = United States Environmental Protection Agency

I. EXECUTIVE SUMMARY

Chevron Phillips Chemical Company LP (CPChem) is committed to fulfilling the High Production Volume (HPV) commitments it made under the U.S. Environmental Protection Agency (USEPA) HPV Challenge Program. As part of this commitment, CPChem has volunteered to assess the health and environmental hazards, including selected physicochemical characteristics of Asphalt, Sulfonated, Sodium Salt (SAS) (CASN 68201-32-1), referred to hereafter as SAS. SAS is a drilling mud additive that is comprised of a diverse distribution of sulfonated alkylaryl hydrocarbon constituents that cross a wide range of molecular weights (500-3000) and are composed of numerous combinations of alkyl and aromatic functional groups with total carbon numbers >25. XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX.

CPChem has identified data from company proprietary files, peer-reviewed literature, and/or calculated endpoints using widely accepted computer modeling programs. In fulfillment with USEPA guidance for use of read-across data (USEPA, 1999b), CPChem proposes the use of surrogate data from similar structural analogues to provide additional support in our understanding of health and environmental hazards for SAS. These surrogate substances include Petroleum-derived salts of Sulfonic Acids, Asphalt, and Alkylaryl Sulfonates. Based on the available physical, chemical, environmental fate, and toxicological data for SAS, these substances demonstrate similar toxicological profiles or follow predictable trends, thus strengthening their use as surrogates.

Physicochemical endpoints for SAS are generally fulfilled by using existing measured data or data calculated by the EPIWIN© computer model. However, additional water solubility testing (per OECD Guideline 105) is proposed for this program. A review of the existing data for SAS and its related structural surrogates shows that sufficient data are available to characterize environmental fate and aquatic toxicity. Level III fugacity modeling predicts that releases of SAS to water would remain in water, releases to soil would remain in soil, and releases to air would partition primarily to soil. Ready biodegradation testing showed that SAS is not readily biodegradable and for additional perspective, SAS has low potential for bioaccumulation in the environment as demonstrated by low predicted octanol solubility, log Pow (n-octanol/water partition coefficient), and fish bioconcentration factors. Acute fish, daphnid, and algal endpoints for SAS are fulfilled with valid study data and demonstrate minimal to low toxicity to aquatic organisms. No additional testing is proposed for environmental fate and ecotoxicity.

Overall, available mammalian toxicity data on SAS (and its structural surrogates that represent many of the SAS functional groups and encompass the most toxicologically significant SAS constituents) indicate a low order of toxicity. SAS has only been tested for acute toxicity via the oral route, where results are of a similar order of magnitude for both SAS and all of the structural surrogates included in this test plan. Acute dermal and inhalation toxicity results for the various structural surrogates likewise demonstrate a low order of toxicity for this class of materials. No additional acute toxicity testing is proposed for this program.

No repeated dose studies on SAS were identified, however, multiple repeated dose toxicity studies are available for SAS surrogates encompassing the alkyl aryl, naphthenic, and asphalt functional groups. In general, results indicated a low order of repeated dose toxicity by the dermal and inhalation routes, however, liver effects in the oral study on Naphthenic Acid indicated that the liver may be a target organ. Neither SAS nor any of its structural surrogates have been tested for reproductive and developmental toxicity. To provide definitive data for SAS, CPChem proposes an OECD Guideline 422 "Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test".

Genotoxicity data exist for all three structural surrogates, Petroleum-derived Sulfonic Acids, Naphthenic Acids, and Asphalts. However, no specific genotoxicity data is available for SAS. CPChem proposes to conduct an AMES Test (OECD 471) to further support the use of surrogate data presented in this test plan.

Table 1 summarizes the available data for SAS and its structural surrogates.

Table 1. Matrix of Available and Adequate Data on SAS and Related Surrogates

Test	SAS	Sulphonic Acid Petroleum Salts (Sur. #1)	Naphthenic Acids (Sur #2)	Asphalt (Sur. #3)	Testing Planned ?
	Y/N				Y/N
Physical and Chemical Data					
Melting Point	Y	Y	Y	Y	N
Boiling Point	Y	Y	Y	Y	N
Vapor Pressure	Y	N	Y	Y	N
Partition Coefficient	Y	N	Y	Y	N
Water Solubility	N	N	Y	Y	Y
Environmental Fate and Pathways					
Photodegradation	Y	N	Y	Y	N
Stability in Water (Hydrolysis)	NA	NA	NA	NA	NA
Transport/Distribution	Y	N	Y	Y	N
Biodegradation	Y	Y	Y	Y	N
Ecotoxicity					
Acute/Prolonged Toxicity to Fish	Y	Y	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	N	N	Y	N
Acute Toxicity to Aquatic Plants (Algae)	Y	N	N	Y	N
Toxicity					
Acute Toxicity (Oral)	Y	Y	Y	Y	N
Acute Toxicity (Inhalation)	N	Y	N	Y	N
Acute Toxicity (Dermal)	N	Y	Y	Y	N

Test	SAS	Sulphonic Acid Petroleum Salts (Sur. #1)	Naphthenic Acids (Sur #2)	Asphalt (Sur. #3)	Testing Planned ?
Repeated Dose	N	Y (Inh. & Derm.)	Y (Oral)	Y (Inh. & Derm.)	Y
GeneticToxicity – *in vitro* Gene Mutation	N	Y	Y	Y	Y
Genetic Toxicity – *in vitro* Chromosomal Aberration	N	Y	Y	Y	N
Genetic Toxicity – *in vivo*	N	N	Y	Y	N
Reproductive Toxicity	N	N	N	N	Y
Developmental Toxicity	N	N	N	N	Y

NA = Not Applicable

NOTE:
The data used to characterize the OECD Screening Information Data Set (SIDS) endpoints for substances in this test plan were identified either in company proprietary files, peer-reviewed literature, and/or calculated using widely accepted computer modeling programs. Surrogates were used for read-across as defined by the USEPA (1999b). All data were evaluated for study reliability in accordance with criteria outlined by the USEPA (1999a). Only studies that met the reliability criteria of "1" (Reliable without restrictions) or "2" (Reliable with restrictions) were used to fulfill OECD SIDS endpoints. Additional data for SAS and the surrogates are also included in the IUCLID (International Uniform Chemical Information Dataset) attached in Appendix I. A more detailed discussion of the data quality and reliability assessment process used in developing this test plan is provided in Appendix II.

II. GENERAL SUBSTANCE INFORMATION

USE: SAS is solely used as an additive for drilling fluids to reduce torque and drag in drilling operations. Under normal operating and use conditions, SAS is not subjected to temperatures greater than 450° F (232°C) as may be expected with asphalts. Exposure to high temperature only occurs in aqueous solution (versus atmospheric conditions) when the SAS-containing drilling fluid is circulated down hole during drilling operations. Upon completion of drilling operations, the drilling fluid is circulated out of the hole and cools as it returns to the surface. The temperature of the drilling fluid being circulated out of the hole ranges from 100-150° F (37-66°C) when it reaches the surface. Under these conditions, fumes are not observed or expected to be emitted from SAS (CPChem Technical Communication, April 2004).

Soltex ® Additive, which uses SAS as the functional ingredient, has been approved for release to the aquatic environment based on data presented in this test plan. This product has been approved by NPDES (National Pollutant Discharge Elimination System) Discharge for oil and gas cutting discharge in Region 9 EPA Gulf Coast Guidelines (40 CFR, Part 435 (a)), and meets OSPAR Convention for the Protection of the Marine Environment in the North-East Atlantic (OSPAR ANNEX 17 (Ref. § 7.4c), Copenhagen: 26 - 30 June 2000).

CHEMISTRY: SAS is a very complex mixture produced by sulfonation of an asphalt-based alkyl aryl hydrocarbon feedstock followed by neutralization of the sulfonated hydrocarbon mixture with sodium hydroxide. This asphalt-based complex alkyl aromatic hydrocarbon mixture ranges in molecular weight from 500-3000 and contains SO_3^- functional groups.

The chemical complexity of SAS comes from the asphalt feedstock, which is naturally variable in composition, and has a wide array of chemical constituents and reactive sites for addition of sulfonic acid functional groups. Asphalt (known as Bitumen in Europe) "is the residuum produced from the non-destructive distillation of crude petroleum at atmospheric pressure and/or under reduced pressures or absence of steam" (Puzinauskas and Corbett, 1978). Asphalts are composed mainly of high-molecular-weight alkylaryl hydrocarbons with high carbon to hydrogen ratios, with carbon numbers > C25, boiling points > 400 °C, high viscosity, and negligible water solubility and vapor pressure. These asphalt alkylaryl hydrocarbons are a heterogeneous mixture of linear, branched and cyclic, saturated and unsaturated, and aromatic functional groups. Importantly, polycyclic aromatic hydrocarbons (PAH) such as benzo(a)pyrene, which are toxicologically significant, are only present in asphalt feedstock at very low concentrations (Phillips Petroleum Company, 1985). Asphalts contain much larger proportions of high-molecular-weight paraffinic and naphthenic hydrocarbons that are substituted with alkyl groups and ultimately sulfonated, which reduces their potential to exhibit PAH-like toxicity (IARC, 1985 in American Petroleum Institute [API], 2003b).

In practice, the asphalt alkylaryl feedstocks are chemically characterized by a saturates, aromatics, resins, and asphaltenes (SARA) analytical technique. Table 2 describes each of these fractions along with the approximate SARA proportions specifically used in SAS production (Witherspoon, 1962; Phillips Petroleum Company, 1985).

Table 2. Description of SARA Profile of Asphalt Feedstock

XXX	Saturates	Consist mainly of long chain saturated hydrocarbons with some branching, alkyl aromatics with long side chains, and cyclic paraffins (napthenes), with molecular weight of 500-1000.
XXX	Aromatic*	Consist mainly of substituted benzene and napthenic-aromatic nuclei with alkyl side chain constituents, with molecular weight range of 500-900.
XXX	Resins	Consist mainly of heterogeneous polar aromatic compounds with small amounts of oxygen, nitrogen, and sulfur, with molecular weight range of 800-2000. Considered lower molecular weight asphaltenes.
XXX	Asphaltenes	Consist mainly of highly condensed aromatic compounds with one or two chromophores containing 4 to 10 fused rings each, with a significant number of alkyl constituents. They have a molecular weight range of 500-1000.

*XXXXXXXXXXXXXX

When the alkylaryl hydrocarbons in the asphalt feedstock are sulfonated during production of SAS, they remain intact and the sulfonation process chemically derivitizes them, converting them into alkylaryl sulfonate sodium salts that still contain carbon

numbers >C25. The sulfonic acid functional groups form by reaction with double bonds in the hydrocarbons, whether on alkyl chains or aromatic rings. The addition of the sulfonic acid group(s) increases the molecular weight, raising melting points >350 °C and boiling points >500 °C, and further reducing vapor pressure versus asphalt. Sulfonation also increases water solubility, or for the higher molecular weight and more hydrophobic constituents, renders them readily dispersible such that they form stable colloidal dispersions or micelles in water.

Understanding that SAS is a complex chemical mixture of alkylaryl sulfonated isomers becomes critically important when characterizing SAS OECD SIDS endpoints. The physicochemical, environmental, and human health properties of SAS will be a function of the specific constituents in any given sample and should be expected to result in ranges versus discrete endpoints for some physical, chemical, and environmental fate properties. Additionally the large molecular size of most SAS constituents will reduce their bioavailability.

Note:XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX.

III. STRUCTURAL SURROGATE DISCUSSION

A. Alkaryl Sulfonates, Asphalts, and Napthenic Acids

CPChem has identified suitable structural surrogates from an array of petroleum-based alkylaryl hydrocarbon products that can be used to support a read-across approach to fulfilling OECD SIDS endpoints for SAS. These are summarized in Table 3 and include specific members of the Alkylaryl Sulfonates, Asphalts, and Reclaimed Substances/Napthenic Acids HPV Categories.

Table 3. Structural Comparison of SAS and HPV Categories that serve as Structural Surrogates for Read-Across Purposes

US HPV Substance Asphalt, Sulfonated, Sodium Salt (SAS) CAS Number 68201-32-1	Generic Structure $\mathbf{R-(SO_3^-\ Na^+)_x}$ R = alkylaryl hydrocarbon with molecular weight = 500-2500 and contains of sulfonic acid groups. Overall Molecular Weight = 500-3000 Total Carbon Number >C25. SAS is the main component in Soltex®

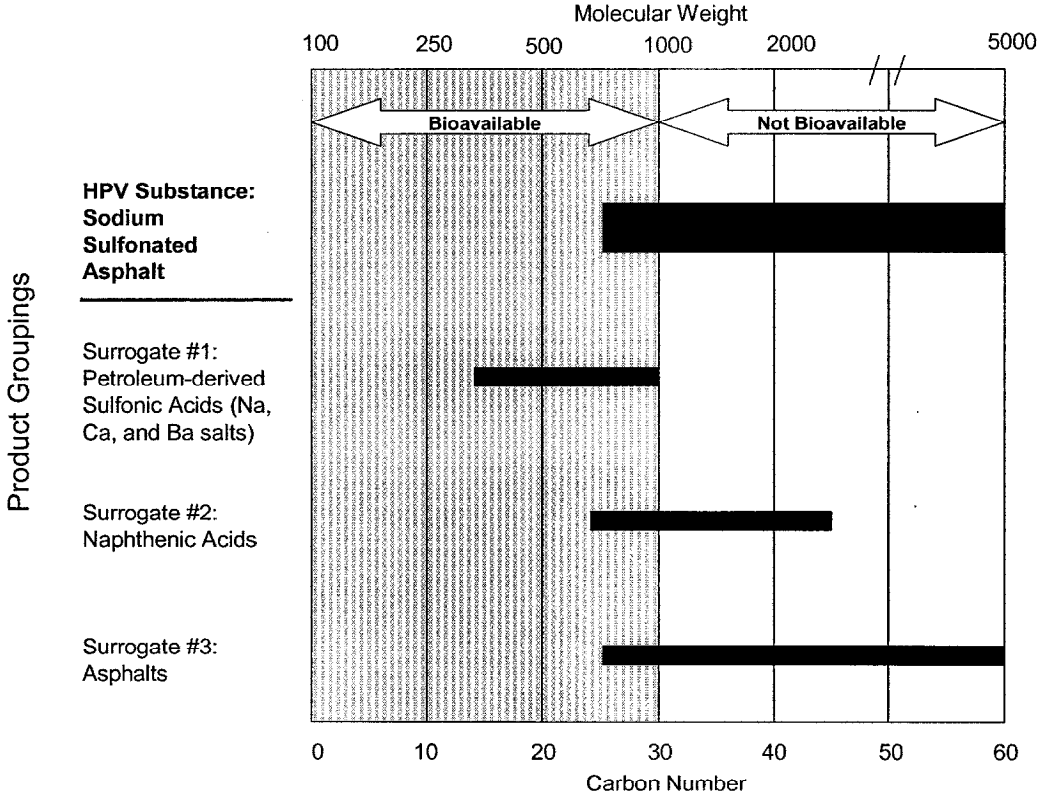
	Additives. (XXXXXX).
Structural Surrogate #1 Sulfonic Acids, petroleum salts CAS Number 68783-96-0 (sodium salt) CAS Number 61789-86-4 (calcium salt) CAS Number 61790-48-5 (barium salt)	Generic Structure: $R-SO_3^- Na^+$ or $(R-SO_3^-)_2 Ca^{+2}$ or $(R-SO_3^-)_2 Ba^{+2}$ R = alkylaryl hydrocarbon with molecular weight = 300-400 Overall Molecular Weight = 300-950 Total Carbon Number >C12-30
Structural Surrogate #2 **Napthenic Acids, Petroleum, crude** CAS Number 64754-89-8	Complex mixture, predominantly of compounds that contain carboxylic acid functional groups and five- to six-member naphthenic rings in their molecular structures. Phenolic compounds and acidic sulfur compounds may also be present. Overall Molecular Weight = 300-950 Total Carbon Number C11->C30
Structural Surrogate #3 **Asphalt Category** CAS Number 8052-42-4 CAS Number 64741-56-6 CAS Number 64742-07-0 CAS Number 64742-16-1 CAS Number 64742-85-4 CAS Number 64742-93-4	Asphalt is the residuum produced from the nondestructive distillation of crude petroleum. Asphalts are complex mixtures of hydrocarbons with molecular weights ranging from 500 to 2000. Overall Molecular Weight = 500-2000 Total Carbon Number Predominantly >C25

Understanding the complex chemical composition of SAS was critical in developing the structural surrogate strategy for this test plan. In evaluating possible structural surrogates for SAS, CPChem considered USEPA HPV criteria for choosing surrogates (USEPA, 1999b), and reviewed a wide range of petroleum-based products that contain similar functional groups to SAS. Importantly, all of the constituents in SAS are at or above the 500-1000 molecular weight range. Due to their larger molecular size and tendency to form micelles or colloids in solution, both of which inhibit biological uptake of the larger SAS molecules, the majority of constituents will not be able to cross cell membranes. In short, they will not be bioavailable to exert systemic toxicity. Regulators at both the USEPA and the European Union have acknowledged this practical molecular weight/molecular size bioavailability cut-off, and have incorporated it into technical guidance for testing and registration of chemicals (Boethling and Nabholz, 1996; EC, 2003).

Figure 1 graphically depicts the alkylaryl sulfonate distribution of SAS constituents versus carbon number and molecular weight range. It also illustrates the bioavailable

lower molecular weight range and shows that most SAS constituents have a large molecular size that will reduce bioavailability and potential for systemic toxicity.

Figure 1. Alkylaryl Sulfonate Distribution of SAS Constituents Versus Carbon Number and Molecular Weight Range (shading indicates bioavailable range)



As described above, SAS comprises a diverse distribution of sulfonated alkylaryl hydrocarbon constituents that cross a wide range of molecular weights (500-3000) and are composed of numerous combinations of alkyl and aromatic functional groups with total carbon numbers >25. The proposed structural surrogates possess these same functional alkylaryl hydrocarbon and/or alkylaryl sulfonate groups.

- **Surrogate #1 Sulfonic Acids, Petroleum Additive Alkaryl Sulfonate Category**

The Sulfonic Acids, petroleum salts category is composed of sodium, calcium, and barium salts of sulfonated alkyl aromatic hydrocarbons. In aqueous conditions the salts will be dissociated, making the same petroleum sulfonic acid ionized species from all three salts forms. This is the most significant surrogate because it overlaps the most bioavailable and therefore toxicologically significant lower molecular weight fraction of SAS constituents, and therefore represents a conservative read-across benchmark for toxicity and ecotoxicity endpoints. One SAS functional group

that is lacking in this category is the naphthenic or polycyclic aromatic sulfonated hydrocarbons, but these functional groups are overlapped by the other proposed surrogates as described below.

- **Surrogate #2 Naphthenic Acids, Reclaimed Substances: Streams Containing Naphthenic Acids Category**

The Naphthenic Acids group adds additional perspective as a read-across surrogate beyond that offered by the Sulfonic Acids, Petroleum salts. They help represent the multicyclic aromatic hydrocarbon fraction of SAS constituents, whereas Surrogate #1 only represents the alkylaryl monocyclic fraction of SAS constituents. The Naphthenic Acids are used in this test plan for read-across for physical/chemical, environmental, and mammalian endpoints. They may contain low levels of sulfonic acid functional groups, but they principally contain carboxylic acid groups, which also impart similarly increased water solubility and reactivity to the alkylaryl hydrocarbon – analogous to the impact of sulfonic acid functional groups on SAS. Overall the Naphthenic Acids represent a conservative read-across benchmark for toxicity and ecotoxicity endpoints since they have a bioavailable fraction. They are relatively nontoxic and are of less concern as a constituent that contributes toward toxicity in the overall SAS product. This illustrates the importance of focusing on the more bioavailable, lower molecular weight fraction of SAS constituents in meaningfully characterizing the SIDS endpoints for SAS.

- **Surrogate #3 Asphalt Category**

CPChem originally intended to include SAS as a member of the HPV Asphalt Category, but abandoned this effort due to dissimilarity arising from the impact of sulfonation on the physical and chemical characteristics of SAS versus nonsulfonated asphalts. However, the Asphalts Category is composed of the same alkylaryl hydrocarbons that are used to make SAS and therefore provides perspective on the environmental fate and toxicological profile of the alkylaryl hydrocarbon functional group in SAS. Importantly the Asphalts Category is predominantly nontoxic and in toxicity tests Asphalt samples were solubilized to maximize bioavailability, which again illustrates that this is a conservative structural surrogate to SAS.

SAS and surrogates #1 (Petroleum Salts of Sulfonic Acids) and #2 (Naphthenic Acids) are characterized by high melting point and boiling point ranges and very low vapor pressures. In the aquatic environment, the SAS sodium salts will be dissociated leaving the ionized species as the environmentally relevant form and surrogates #1 and #2 would also be dissociated in aqueous conditions further demonstrating their suitability as surrogates.

IV. PHYSICOCHEMICAL PROPERTIES

Importantly, SAS and its structural surrogates are complex heterogeneous mixtures containing many different sulfonated alkylaryl isomers as described above. Therefore, physicochemical properties may vary according to proportions of individual constituents in the sample tested, which results in these substances having ranges rather than discreet melting and boiling points or vapor pressures. Only limited physicochemical testing has been completed for SAS, as summarized in Table 4. Calculations using EPIWIN (USEPA and Syracuse Research Corporation, 2000) are also provided where representative alkylaryl hydrocarbon chemical structures were developed for SAS constituents in the carbon number range of C26-C41. The representative structures are presented in Tables 4a, 5a, and 5b, and are discussed further in subsequent sections.

The physical chemical data for SAS and its HPV Category surrogates provided in Table 4 were experimentally measured or calculated using EPIWIN.

Table 4. Measured and Calculated Physicochemical Properties

Physical and Chemical Data				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts (Sur. #1)**	**Napthenic Acids (Sur. #2)**	**Asphalts (Sur. #3)**
Melting Point	See Table 4a	349.84 °C[1]	117 to 160 °C[3]	ND
Boiling Point	>500 °C[7]	935.88 °C[1]	233 to 375 °C[3]	>450 °C[2]
Vapor Pressure	Negligible[7]	$<1X10^{-10(1)}$	1.4×10^{-5} to $1.8 \times 10^{-3(3)}$	Negligible[2]
Kow Partition Coefficient	< 0, 1.1, 3.2, and > 6.2[5] <0[6]	ND	5.1 to 9.2[4]	≥10.0[4]
Water Solubility	ND	ND	0.0003 to 2.1[4]	ND

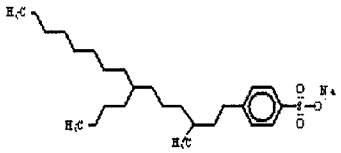
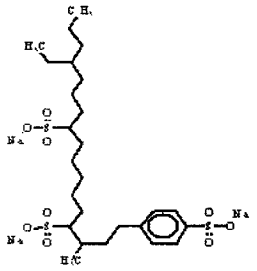
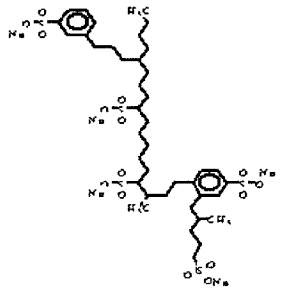
[1]ACC, 2001.
[2]API, 2003d.
[3]EPIWIN v3.10; MPBPWIN v1.40.
[4]EPIWIN v3.10; calculated using WSKOW v1.40.
[5]TNO Environmental and Energy Research (TNO), 1997.
[6]Chemex Environmental International Limited, 2003.
[7]CPChem internal communication
ND = No Data Available

To help further characterize the SAS SIDS physicochemical and environmental fate endpoints and the trends across the expected range of SAS constituents, three representative sulfonated alkylaryl hydrocarbon chemical structures were developed where carbon number and degree of sulfonation were varied. These are representative of SAS constituents across the carbon number range of C26-C40, as summarized in Table 4a and entered into EPIWIN as follows:

1. A C26 monosulfonated species representing the low end of the molecular weight range of SAS.
2. A C26 trisulfonated species representing a polysulfonated C26 constituent and to illustrate the impact of increasing sulfonation alone versus monosulfonated (#1).
3. A C40 penta-sulfonated species representing the higher end of the carbon number and sulfonic acid group substitution.

In general, increased sulfonation increases boiling points and is expected to increase melting points (EPIWIN can not estimate melting points > 349.84 °C.) Increased sulfonation will also further reduce vapor pressure. Therefore, calculated values for monosulfonated isomers are used for SAS with reporting as greater than "the monosulfonated representative structure" to indicate that there will be a range or that some fraction will decompose.

Table 4a. EPIWIN Physicochemical Data for Representative Structures

Physical and Chemical Data			
Parameter	 ($C_{26}H_{43}O_9S_3Na_3$)	 ($C_{26}H_{45}O_3SNa$)	 ($C_{40}H_{61}O_{15}S_5Na_5$)
Melting Point	> 349.84 °C [1]	>349.84 °C[1]	>349.84 °C[1]
Boiling Point	739.46 °C [1]	916.13 °C[1]	1276.77 °C[1]
Vapor Pressure	6.02×10^{-18} mmHg at 25 °C [1]	3.9×10^{-23} mmHg at 25 °C [1]	1.75×10^{-33} mmHg at 25 °C [1]
Kow Partition Coefficient	6.78 [2]	2.32 [2]	4.05 [2]
Water Solubility	0.002071 milligrams per liter (mg/L) at 25 °C [2]	0.6256 mg/L at 25 °C [2]	4.655×10^{-5} mg/L at 25 °C [2]

[1] EPIWIN v3.10; MPBPWIN v1.40.

[2] EPIWIN v3.10; calculated using WSKOW v1.40.

These EPIWIN data show that SAS and its surrogates will have high melting point ranges (>349.84 °C), boiling point ranges > 900 °C, and very low vapor pressures. SAS has a water soluble fraction and is water dispersible by design. Therefore, a water solubility continuum will occur in which SAS fractions may be soluble across a range from ppm to zero. The water solubility measurements were operationally defined and not pursuant to USEPA or Organisation for Economic Cooperation and Development (OECD) guidelines. Importantly, the functional groups in SAS constituents are not labile to hydrolysis. The high degree of sulfonation will significantly increase water solubility and reduce octanol solubility such that SAS constituents will have a very low Kow, where Kow values can range from 2 to 7, and which suggests there is low cause for concern for bioaccumulation in aquatic organisms.

Summary: The weight of evidence supports that adequate data (i.e., Klimisch rating 1 and 2) are available for most physical and chemical endpoints; additional water solubility testing is proposed for the USEPA HPV Challenge Program (see Tables 4 and 4a and IUCLID documents).

V. EVALUATION OF ENVIRONMENTAL FATE DATA

SAS and its structural surrogates are complex heterogeneous mixtures containing many different sulfonated alkylaryl isomers, as described above. Therefore, environmental fate properties will vary according to the relative proportions of specific functional groups in the sample tested, which results in these substances having ranges rather than discreet environmental fate endpoints such as rate constants, reaction profiles, or partitioning behavior. This complexity especially confounds whole SAS product fugacity modeling since SAS constituents will be subject to differential partitioning depending on the degree of sulfonation and overall carbon content, etc.

Environmental fate data for SAS were either experimentally measured or estimated using representative structures in EPIWIN, and are provided in Tables 5, 5a, and 5b.

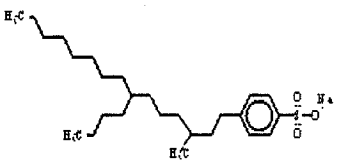
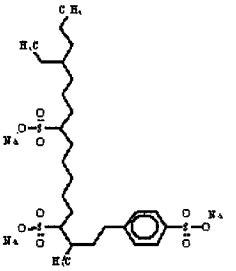
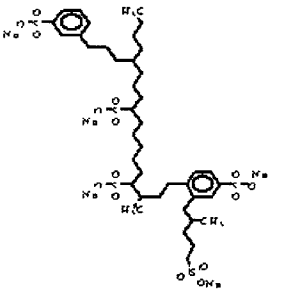
Table 5. Measured and Calculated Results for Environmental Fate and Pathways

Environmental Fate and Pathways				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts Na (Sur. #1)**	**Napthenic Acids (Sur. #2)**	**Asphalts (Sur. #3)**
Photodegra-dation and Atmospheric Oxidation: • OH Half Life	See Table 5a	ND	0.3 to 0.6 days[5]	Physicochemical characteristics do not favor distribution to environmental compartments where photodegradation

Environmental Fate and Pathways				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts Na (Sur. #1)**	**Napthenic Acids (Sur. #2)**	**Asphalts (Sur. #3)**
				reactions will occur.[7]
Stability in Water (Hydrolysis)	No Data, Low Potential	Low Potential[1,2]	Components do not undergo hydrolysis – no testing proposed[6]	Category does not undergo hydrolysis.[7]
Transport/ Distribution Fugacity Estimated Koc: Estimated BCF:	See Table 5b See Table 5a See Table 5a	ND	NA	Tend to remain intact and within the medium in which they were released.[7]
Biodegra-dation	3-6% in 28 days[3] 0% in 56 days[4]	8.6% biodegraded after 28 days[1]	6-7%[6]	Under realistic exposure conditions where the bulk properties of asphalt limits dispersion and the available surface area for microbial exposure, biodegradation is expected to be minimal.[7]

[1]ACC, 2001.
[2] Based on Functional Group and Chemical Class: Branched hydrocarbon chain (CAS N 61789-86-4); linear hydrocarbon chain (CAS N 68783-96-0); and sulfonic acid (CAS N 61790-48-5).
[3]TNO, 1991b.
[4]TNO, 1993.
[5]EPIWIN v3.10; calculated using AOP Program v1.90.
[6]API, 2003c.
[7]API, 2003d.
NA = Not Applicable.
ND = No Data Available.

Table 5a. EPIWIN Environmental Fate and Pathways Data for Representative Structures

Physical and Chemical Data			
Parameter	 ($C_{26}H_{43}O_9S_3Na_3$)	 ($C_{26}H_{45}O_3SNa$)	 ($C_{40}H_{61}O_{15}S_5Na_5$)
Photodegradation and Atmospheric Oxidation:			
• OH Rate Constant	28.4858 x 10^{-12} cm^3/molecule-sec[1]	31.5298 x 10^{-12} cm^3/molecule-sec[1]	45.0897 x 10^{-12} cm^3/molecule-sec[1]
• OH Half Life	4.506 Hrs[1]	4.071 Hrs[1]	2.847 Hrs[1]
Transport/ Distribution			
Fugacity	See Table 5b	See Table 5b	See Table 5b
Estimated Koc:	1.821 x 10^{6} [(2)]	9.466 x 10^{7} [(2)]	1 x 10^{10} [(2)]
Estimated BCF:	70.79[3]	70.79[3]	70.79[3]

[1]EPIWIN v3.10; calculated using AOP Program v1.90.
[2]EPIWIN v3.10; calculated using PCKOC Program v1.66.
[3]EPIWIN v3.10; calculated using BCF Program v2.14.

Summary: The weight of evidence in this test plan supports that no further testing is necessary to meet HPV SIDS endpoints relating to environmental fate. Adequate data (i.e., Klimsch rating 1 and 2) are available for all endpoints; no additional testing is proposed for the USEPA HPV Challenge Program (See Tables 5, 5a, and 5b and IUCLID documents). SAS is expected to be labile and mobile if released to the environment, but will disappear based upon both biotic and abiotic degradation mechanisms. SAS does not pose any bioaccumulation hazard, as described in detail below.

A. Photodegradation – Atmospheric Oxidation

Constituents of SAS are polyaromatic and act as chromophores (which absorb light energy in the 290 nm to 800 nm range where photolytic reactions may result). The degree and rate at which these compounds undergo direct photolysis is a function of the light intensity at site of the SAS molecules. Also, indirect photodegradation may occur in the atmosphere where the SAS constituents interact with photochemically produced hydroxyl radicals, ozone, or nitrogen oxides. Hydrocarbons, such as the alkylaryl hydrocarbons in SAS, react readily with OH^- and NO_3 radicals, and monochromatic and dichromatic compounds react readily with OH^- radicals to undergo degradative reactions (Atkinson, 1990 in API, 2003b). However, due to the fact that SAS and its sulfonated structural surrogates have very low vapor pressures, they do not have a tendency to volatilize to air where they can undergo reactions with photosensitized oxygen in the form of hydroxyl radicals (OH^-). As a result, these reactions are not expected to be significant environmental fate processes.

Values for SAS photodegradation and atmospheric oxidation were calculated based upon representative chemical structures using EPIWIN, and are shown in Table 5a. A calculated half-life for SAS of 3 to 5 hours and rate constant of 28×10^{-12} - 45×10^{-12} cubic centimeters (cm^3)/molecule-sec has been estimated using EPIWIN for reaction with hydroxyradicals.

Summary: These results show that SAS may be subject to photodegradation and atmospheric oxidation, and are sufficient for USEPA HPV Challenge Program purposes; no further testing is warranted.

B. Hydrolysis

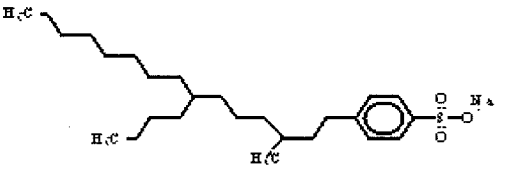
Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Harris, 1982 in API, 2003a). Because SAS does not contain significant levels of these functional groups, components in SAS are not subject to hydrolysis.

Summary: Components in SAS do not undergo hydrolysis. Existing information is sufficient for USEPA HPV Challenge Program purposes; no further hydrolysis testing is warranted.

C. Chemical Transport and Distribution in the Environment (Fugacity Modeling)

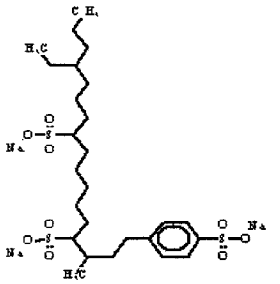
EPIWIN produced the following Level III Fugacity results for the representative structures to SAS:

Table 5b. EPIWIN Level III Fugacity Results for Representative Structures



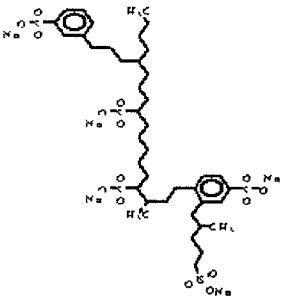
(C_{26} H_{43} O_9 S_3 Na_3)

Compartment	100% to air	100% to water	100% to soil	Equally to each compartment
Air	5.33%	0.000131%	0.00%	0.444%
Water	2.47%	12.3%	0.00161%	8.2%
Soil	74.7%	0.00183%	100%	33.1%
Sediment	17.5%	87.7%	0.0114%	58.2%



(C_{26} H_{45} O_3 S Na)

Compartment	100% to air	100% to water	100% to soil	Equally to each compartment
Air	0.0055%	0.00%	0.00%	0.35%
Water	10.3%	99.5%	5.66%	31.5%
Soil	89.6%	0.00%	94.3%	68.0%
Sediment	0.0557%	0.537%	0.0306%	0.17%



(C_{40} H_{61} O_{15} S_5 Na_5)

Compartment	100% to air	100% to water	100% to soil	Equally to each compartment
Air	0.00%	0.00%	0.00%	0.00246%
Water	3.55%	82.3%	0.156%	15.3%
Soil	95.7%	0.00%	99.8%	81.4%
Sediment	0.763%	17.7%	0.0334%	3.29%

Summary: Results from the Level III fugacity modeling indicate that releases of SAS to water would remain in water, while releases to air would partition primarily to soil. Likewise, releases to soil would remain in soil. Further fugacity modeling is not warranted for the USEPA HPV Challenge Program.

D. Biodegradation and Bioaccumulation

SAS has been tested in two Ready Biodegradation tests in seawater according to proposed EC test guidelines and was not readily biodegradable (3 to 6% in 28 days and 0% in 56 days) in both studies. The results are reliable without restrictions and fulfill the HPV SIDS endpoint for SAS.

In addition, the EPIWIN predicted bioconcentration factor (BCF) for representative structures to SAS were 70.79 and the organic carbon partition coefficients (Koc) were 1.8×10^6 to 1×10^{10}. The BCF should be low, but the BCF QSAR defaults to a low BCF for substances that are expected to be ionized in aqueous media. Overall these results indicate that SAS will be sorptive and poses a low bioaccumulation potential.

Summary: Adequate biodegradation data are available; no additional biodegradability testing is proposed for the USEPA HPV Challenge Program (See Table 5 and IUCLID documents).

VI. ECOTOXICITY DATA

Acute fish, daphnid, and algal endpoints for SAS are fulfilled with valid study data. The studies were conducted consistent with relevant OECD and USEPA guidelines that were revised to marine species testing conditions. Marine species were chosen due to the fact that SAS is primarily used in off-shore drilling and therefore, marine species are the most relevant species. As shown in Table 6, SAS is virtually nontoxic to aquatic organisms.

Aquatic toxicity studies have been performed on marine fish, invertebrates, and algae, showing a low order of aquatic toxicity for SAS; fish appear to be the most sensitive species with 72 and 96 hour LC_{50} data showing toxicity at 1,672 mg/L.

Table 6. Results for Ecotoxicity Endpoints

Ecotoxicity Endpoints				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts (Sur. #1)**	**Napthenic Acid (Sur. #2)**	**Asphalt (Su. #3)**
Acute/	24- and 48-hr LC_{50}	96-hr LL_0 =	96-hr TLm =	LC_{50} >1000

Ecotoxicity Endpoints				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts (Sur. #1)**	**Napthenic Acid (Sur. #2)**	**Asphalt (Su. #3)**
Prolonged Toxicity to Fish	>1,800 mg/L, and 72- and 96-hr LC_{50} = 1,672 mg/L[4, S]	10,000 mg/L[5,C]	16.3 mg/L (ppm) [6,B] 96-hr LC50 ~ 5 mg/L[6,G]	mg/L (structural analogs C15 and greater)[7,O]
Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	96-hr LC_{50} = 420,000 ppm[1,M]	ND	ND	LC_{50} >1000 mg/L (structural analogs C15 and greater) [7, D]
Acute Toxicity to Aquatic Plants (Algae)	NOEC = 1.0 grams per liter (g/L)[3,K] EC_{50} = 4.0 g/L[3,K]	ND	ND	LC_{50} >1000 mg/L (structural analogs C15 and greater) [7,P]
Other	Not toxic[2,N] 96-hr LC_{50} = 155,000 ppm (liquid phase bioassay) and 205,000 ppm (suspended particulate phase bioassay)[2,A]	ND	ND	ND

[1]Laboratory Technology, Inc., 1994.
[2]Marine Bioassay Laboratories, 1982.
[3]TNO, 1991a.
[4]Chemex Environmental International Limited, 2002.
[5]ACC, 2001. WAF (Water accommodated fraction static nonrenewal test.)
[6]API, 2003c.
[7]API, 2003d.
ND = No Data Available
[A]*Acanthomysis sculpta* (shrimp-like Mysids)
[B]*Brachydanio rerio* (Zebra Fish)
[C]*Cyprinodon variegatus* (Sheepshead Minnow)
[D]*Daphnia magna*
[G]*Gasterosteus aculeatus* (Three-spine Stickleback)
[K]*Skeletonema costatum*
[M]*Mysidopsis bahia* (Mysid shrimp)
[N]*Macoma nasuta* (Mollusca)
[O]*Oncorhynchus mykiss*
[P]*Selenastrum capricornutum*
[S]*Scophthalmus maximus* (Turbot)

Summary: Adequate aquatic toxicity data are available for SAS; no additional testing is proposed for the USEPA HPV Challenge Program (see Table 6 and IUCLID document).

VII. MAMMALIAN TOXICITY

Overall, available mammalian toxicity data on SAS, and its structural surrogates that represent many of the SAS functional groups and encompass the most toxicologically significant SAS constituents, indicate a low order of toxicity. SAS has only been tested for acute toxicity via the oral route, where results are of a similar order of magnitude for both SAS and all of the structural surrogates included in this test plan. This helps reinforce the suitability of using these surrogates as benchmarks for SAS. Acute dermal and inhalation toxicity results for the various structural surrogates likewise demonstrate a low order of toxicity for this class of materials. Repeated dose studies were identified for all three surrogates (dermal and inhalation studies for Surrogate #1, Ca salts of Petroleum-derived Sulfonic Acids; an oral study for Surrogate #2, Naphthenic Acids; and dermal and inhalation studies for Surrogate #3, Asphalts). In general, results indicated a low order of repeated dose toxicity by the dermal and inhalation routes, however, liver effects in the repeated dose oral toxicity study on Naphthenic Acid indicated that the liver may be a target organ. Neither *in vitro* nor *in vivo* genetic toxicity studies were identified for SAS. However, *in vitro* studies (both gene mutation and chromosomal aberration studies) were negative for all of the structural surrogates, with the exception of the Asphalts (Surrogate #3) where studies demonstrated that whole asphalts are nonmutagenic or are weakly mutagenic and that fume condensates are mutagenic with the severity of the effect correlating with the temperature under which the fumes are generated (API, 2003b). *In vivo* genetic toxicity studies were identified for Surrogates #1 (Ca salts of Petroleum-derived Sulfonic Acids) and #3 (Asphalts). While the Sulfonic Acids were found not to be genotoxic, conflicting results were reported for the Asphalts. No reproductive or developmental studies were identified for SAS or any of its structural surrogates.

Table 7. Results for Mammalian Toxicity Endpoints

Mammalian Toxicity Endpoints				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts (Sur. #1)**	**Napthenic Acid (Sur. #2)**	**Asphalts (Sur. #3)**
Acute Oral	>5,000 milligrams per kilogram (mg/kg) bw (rat – m and f)[1, 2]	Na Salt: LD_{50}>5,000 mg/kg (rat).[3] Ca Salt: LD_{50}>5,000 mg/kg (rat).[3] Ba Salt: LD_{50}>2,000 mg/kg (rat).[3]	1. LD_{50} = 5,880 mg/kg (rat).[5] 2. LD_{50} = 3,000 mg/kg (rat) – fraction from crude kerosene acids[5] and	LD_{50} > 5,000 mg/kg bw (rat).[6]

Mammalian Toxicity Endpoints				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts (Sur. #1)**	**Napthenic Acid (Sur. #2)**	**Asphalts (Sur. #3)**
			LD_{50} = 5,200 mg/kg (rat) – fraction from mixed crude oils.[5] 3. High dose effects (300 mg/kg bw): decreased food consumption; lethargy and mild ataxia; signif. inc. in relative organ weights of ovaries and spleen (female) and testes and heart (male); eosinophilic pericholangitis, and brain hemorrhage.[5]	
Acute Inhalation	ND	Na Salt: LC_0 > 1.9 mg/L (rat).[3,4]	ND	LC_{50} >94.4 mg/m^3 (rat).[6]
Acute Dermal	ND	Na Salt: LD_{50}>2,000 mg/kg (rabbit).[3] Ca Salt: LD_{50}>5,000 mg/kg (rabbit).[3]	LD_{50} = 3160 mg/kg (rabbit).[5]	LD_{50} >2,000 mg/kg bw (rabbit).[6]
Repeat Dose – Oral	ND	ND	NOAEL and LOAEL not provided, see description in Section B below.[5]	ND
Repeat Dose – Dermal	ND	Ca Salt: NOAEL = 1,000 mg/kg/day (highest dose tested) (rat – 28 day).[3]	ND	Rabbit Study – NOAEL and/or LOAEL not provided, see description in Section B below.
Repeat Dose – Inhale.	ND	Ca Salt: NOAEL = 49.5 milligrams per cubic meter (mg/$m^{3)}$ (rat – 28 day).[3]	ND	NOAEL = 28.17 mg/m^3 (rat).[6,7]
Genetic (*In vitro*) Gene Mutation	ND	Ca Salt: Bacterial Reverse Mutation Assay – not mutagenic – genotoxicity NOEL = 5,000 micrograms per plate (µg/plate).[3] Ca Salt: Mouse Lymphoma Mutagenicity Screen – not mutagenic.[3]	Negative (Ca and Na salts) – with and without activiation.[5]	Whole asphalts are nonmutagenic or weakly mutagenic, fume condensates are mutagenic (severity correlates with temperature under which fumes are generated).[7]

Mammalian Toxicity Endpoints				
Test	**SAS**	**Sulfonic Acids, Petroleum Salts (Sur. #1)**	**Napthenic Acid (Sur. #2)**	**Asphalts (Sur. #3)**
Genetic (*In vitro*) Chrom. Aberr.	ND	Ca Salt: CHO Cell Chromosomal Aberration Assay – not genotoxic.[3]	Negative (Na salt)[5] (Na salt was positive in sister chromatid exchange assay).[5]	Roofing asphalt fumes caused a dose-related increase in micronucleus formation in Chinese Hamster lung fibroblasts.[7] Three paving asphalt fume condensates were negative in an unspecified chromosome aberration assay.[7]
Genetic – *In vivo*	ND	Ca Salt: Mouse Micronucleus Assay – not genotoxic – genotoxicity NOEL = 2,000 mg/kg.[3]	ND	1. Two negative oral chromosome aberration studies on vacuum residuum samples.[7] 2. Increased micronucleus formation in bone marrow erythrocytes.[7] 3. Positive dermal and intratracheal instillation DNA adduct tests.[7]
Repro-duction/ Develop-mental Screen	ND	ND	ND	ND

[1]Hazleton Laboratories American, Inc., 1985a.
[2]Hazleton Laboratories American, Inc., 1985b.
[3]ACC, 2001.
[4]LC_0 = no mortality observed at the highest concentration tested.
[5]API, 2003c.
[6]API, 2003d.
[7]API, 2003b.
ND = No Data Available

Summary: Sufficient acute toxicity data are available for SAS and/or its surrogates. No further acute toxicity testing is proposed. Repeated dose studies were identified for all three surrogates (dermal and inhalation studies for Surrogate #1, Ca salts of Petroleum-derived Sulfonic Acids; an oral study for Naphthenic Acids; and dermal and inhalation studies for Surrogate #3, Asphalt). While multiple repeated dose toxicity studies are available, which encompass the alkylaryl, naphthenic, and asphalt functional groups, these data do not entirely address this endpoint for SAS. In addition, no reproductive or developmental studies were identified for SAS or any of its structural surrogates. To fulfill the repeated dose, reproductive, and developmental toxicity endpoints, a 28-day combined, repeated dose and reproductive/developmental toxicity screening study (OECD Guideline 422) is proposed. Genotoxicity data exist for all three structural surrogates. However, no specific genotoxicity data is available for SAS. CPChem proposes to conduct an AMES Test (OECD 471) to further support use of surrogate data presented in this test plan.

(See Table 7 and IUCLID Documents.)

A. Acute Toxicity

SAS demonstrated a low order of toxicity via the oral route of exposure (LD_{50} > 5,000 mg/kg body weight). Consistent results were seen for the three structural surrogates: the Na, Ca, and Ba salts of Petroleum-derived Sulfonic Acids (Surrogate #1); the Naphthenic Acids (Surrogate #2); and the Asphalts (Surrogate #3), as demonstrated in Table 7 above. In addition, acute dermal toxicity data for the various structural surrogates indicate that SAS would be expected to have a very low order of acute toxicity via this route as well (LD_{50} of 2,000 to 5,000 mg/kg in rabbits for Surrogate #1 [Na and Ca salts of Petroleum-derived Sulfonic Acids] and Surrogate #3 [Asphalts]). Limited data exist regarding the acute inhalation toxicity of this class of material. No acute inhalation toxicity data were identified for SAS, however an LC_0 of 1.9 mg/L (the maximum attainable concentration) was reported in rats exposed to Na salts of Petroleum-derived Sulfonic Acid and an LC_{50} of 9.4 mg/m^3 was reported for asphalt condensate fumes. Due to the low vapor pressure of SAS, exposure via the respiratory route is unlikely. As a result, the low order to toxicity demonstrated by the asphalt condensate fumes is expected to be a conservative benchmark for SAS.

Summary: These studies fulfill the HPV requirements for the acute toxicity endpoint; no additional testing is proposed for the USEPA HPV Challenge Program.

B. Repeated Dose Toxicity

No repeated dose toxicity data were identified for SAS. However, both a dermal and inhalation repeated dose study were identified for Surrogate #1 – Ca salts of Petroleum-derived Sulfonic Acids. In a 28-day dermal repeated dose study following OECD Guideline 410, a NOAEL of 1,000 mg/kg was established (highest dose

tested) and no signs of overt systemic toxicity were demonstrated. In a 28-day inhalation repeated dose study following OECD Guideline 412, a NOAEL of 49.5 mg/m^3 was established based on the slight, dose-related increase observed in the severity of microscopic pulmonary findings and increased lung weights.

A 90-day oral subchronic study in rats was identified for Surrogate #2, Naphthenic Acid (in aqueous solution, derived from Athabasca sands tailings). While neither a NOAEL or an LOAEL were reported, the following results were provided:

- Significant effects in the high dose group (60 mg/kg bw) included decreased food consumption immediately following dosing; severe, clonic seizures lasting 20 seconds in 25% of dosed animals (observed after day 40) – after which all animals, except one that died, resumed normal activity; lower mean body weight throughout the exposure period; increased relative organ weights in the liver, kidney, and brain; reduction in plasma cholesterol on days 45 and 91 (41 and 43%); increase in amylase activity on day 45 and 91 (33 and 30%); less pronounced differences in total protein concentration (increased) and albumin/globulin ratio (decreased); and five out of 12 rats with increased glycogen storage. Results indicate that the liver is likely a target organ.
- Significant effects in mid-dose group (6 mg/kg bw) included severe, clonic seizures lasting 20 sec in 17% of dosed animals (observed after day 40) – after which all animals, except one that died, resumed normal activity; and three out of 12 rats with increased glycogen accumulation.
- Significant effects in low-dose group (0.6 mg/kg bw) were minimal with only two out of 12 rats exhibiting increased glycogen accumulation.

Two 28-day dermal repeated dose toxicity studies in male and female New Zealand white rabbits were identified for Asphalt (Surrogate #3). In both studies, the rabbits were treated with 200, 1,000, and 2,000 mg/kg vacuum residuum samples API 81-13 and API 81-14 undiluted and occluded, once a day, three times a week for 4 weeks (API, 2003b). While neither a NOAEL nor a LOAEL were reported for either study, the following results were provided:

- Treatment-related clinical signs in animals that survived to day 28 (two animals died and two were sacrificed moribund during the study but none of these were considered to be compound-related) included thin appearance, decreased food intake, flaking skin, and wheezing.
- Edema was recorded in all groups except controls throughout the study; severity ranged from very slight to slight. Erythema could not be scored at most daily intervals because the test material could not be removed from the skin and therefore obscured the test site.
- At 2,000 mg/kg, a treatment-related suppression in body weight gain was recorded for the high dose male groups. Rabbits appeared thin, experienced decreased body weight gain, and decreased food intake. Significant differences included absolute kidney weight in males (-16%), absolute/

relative right adrenal weight in males (+ 86/133%), absolute pituitary weight in females (+63%), and relative spleen weight in females (+50%).

- At 1,000 mg/kg, significant differences were reported in male kidney weights (-14%).
- Flaking skin, acanthotic dermatitis, and hyperkeratosis were seen in males given 2,000 mg/kg API 81-13, and in both sexes, API 81-14 also produced wart-like lesions and white discharge at the treated site.
- No treatment-related trends in any of the hematological or clinical chemical parameters that were measured were reported.
- No systemic toxicity was reported.

A 90-day subchronic inhalation toxicity study following OECD Guideline 413 was also identified for Asphalt (Surrogate #3). In this study, male and female Wistar rats were exposed (nose-only) to asphalt fume condensate collected over a paving asphalt tank. Target concentrations were 0, 4, 20, and 100 mg/m^3. Actual mean concentrations measured by IR according to BIA (Germany) guideline #6305 and corrected for aromatic content (Ekström et al., 2001 in API, 2003), were 5.53, 28.17, and 149.17 mg/m^3 total hydrocarbon of bitumen fumes. The following results were provided:

- At 149.17 mg/m3, male rats exhibited statistically significant lower body weights with a concurrent decrease in food consumption, and female rats had slightly lower body weights than controls.
- Histopathological changes were observed in the nasal and paranasal cavities in both sexes.
- Broncho-alveolar lavage demonstrated a statistically significant increase in mean cell concentration, lactate dehydrogenase levels, and alpha glutamyl transferase levels in high dose female rats; effects in high dose males were similar but less pronounced.
- The NOAEL for this study was 28.17 mg/m^3 (API, 2003b).

Summary: While multiple repeated dose toxicity studies are available for SAS surrogates encompassing the alkylaryl, naphthenic, and asphalt functional groups, these data presented do not entirely address this endpoint for SAS. A 28-day combined, repeated dose, and reproductive/developmental toxicity screening study (OECD Guideline 422) is proposed.

C. Genetic Toxicity/Mutagenicity

1. *In Vitro* Gene Mutation and Chromosomal Aberration Studies

No studies were identified for SAS. However, gene mutation tests conducted on Ca salts of Petroleum-derived Sulfonic Acids (Surrogate #1) and the Ca and Na salts of Naphthenic Acid (Surrogate #2) consistently resulted in negative results using the Ames Test. Surrogate #1 was also tested in the mouse lymphoma mutagenicity screen test and was found not to be mutagenic. *In vitro* chromosomal aberration test results were identified as well for Surrogates #1 and

#3. Ca salts of Petroleum-derived Sulfonic Acids (Surrogate #1) were found to be "not genotoxic" in the CHO cell chromosomal aberration assay. Likewise, a study on the Na salt of Naphthenic Acid (Surrogate #2) was also found to be negative in a chromosomal aberration test conducted by the National Toxicology Program (API, 2003a).

Ambiguous results were reported for Asphalt (Surrogate #3). In general, *in vitro* studies demonstrated that whole asphalts are nonmutagenic or are weakly mutagenic, and that fume condensates are mutagenic with the severity of the effect correlated with the temperature under which fumes are generated. Asphalt fumes generated at > 232°C (>450°F) exhibited moderate mutagenicity while asphalt fumes generated at 163 C (325°F) exhibited lower mutagencitiy (API, 2003b).

In contrast to asphalt, SAS does not emit fumes during its normal intended use (typical surface temperatures during drilling operations ranges between 100-150° F (37-66°C)). CPChem proposes an initial genotoxicity screen using Ames Test (OECD 471) for 3 reasons. 1) similar sensitivities of detecting a positive genotoxic insult have been described for the *in vitro* Ames Test versus the rodent micronucleus assay; furthermore animal use is minimized, 2) a potential exists for osmotic/ionic disruptions to occur in the *in vitro* chromosome aberration test caused by the sodium salt of SAS; hence increasing the possibility of false positive results (2004 Mid America Toxicology Course Syllabus; oral communication with D.J. Brusick), and 3) as an initial screen to strengthen SAR data (currently negative genotoxicity with the exception of contradicting asphalt fume data) presented in this test plan and/or future surrogate data being generated through the US HPV Challenge Program.

Summary: CPChem proposes to conduct an Ames Test (OECD 471).

2. *In Vivo* Genetic Toxicity/Mutagenicity

No studies were identified for SAS. However, Ca salts of Petroleum-derived Sulfonic Acids (Surrogate #1) were found to be "not genotoxic" in the mouse micronucleus assay. However, *in vivo* studies for Asphalt (Surrogate #3) presented conflicting results. *In vivo* genetic toxicity data included two negative oral chromosome aberration studies on vacuum residuum samples, a micronucleus test in which asphalt fume condensate instilled intratracheally induced increased micronucleus formation in bone marrow erythrocytes, and positive dermal and intratracheal instillation DNA adduct tests. Sponsors of the Asphalt Category indicate that the conflicting results in the *in vivo* cytogenetic assays presented above should be resolved by an ongoing micronucleus evaluation being conducted in rats exposed to bitumen fumes in an ongoing lifetime inhalation study (API, 2003b).

Summary: No Testing proposed. Based on results from the *in vitro* Ames Test mentioned above, CPChem may find that further testing is required using the *in vivo* mouse micronucleus test (OECD 474).

D. Reproductive/Developmental Toxicity

No reproductive or developmental toxicity studies were identified for SAS or any of its structural surrogates (with the exception of a reproductive toxicity study for Surrogate #3 [Naphthenic Acid], which was not of sufficient data quality and was in abstract form only) (API, 2003a). However, considering the high molecular weight, limited bioavailability, and minimal observed general toxicity of SAS, SAS is unlikely to cause developmental or reproductive effects.

Summary: Given that no data are available for the reproductive and developmental toxicity endpoints and to provide definitive data for SAS, testing is proposed following OECD Guideline 422 "Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test".

VIII. CONCLUSIONS

As summarized below, adequate data (i.e., Klimisch rating 1 and 2) are available for several endpoints. However, testing is proposed for the following endpoints:

- water solubility;
- repeated dose toxicity;
- *in vitro* genetic toxicity/mutation;
- reproduction toxicity; and
- developmental toxicity.

PHYSICOCHEMICAL DATA. EPIWIN data show representative structures to SAS and its surrogates will have high melting point ranges (>349.84 °C), boiling point ranges > 900 °C, and very low vapor pressures. SAS has a water soluble fraction and is water dispersible by design; therefore a water solubility continuum will occur in which SAS fractions may be soluble across a range from ppm to zero. Importantly, the high degree of sulfonation significantly reduces octanol solubility such that SAS constituents will have a very low Kow, where Kow values can range from 2 to 7, which suggests that there is low cause for concern for bioaccumulation. The weight of evidence supports that adequate data are available for the physicochemical endpoints, with the exception of water solubility. For the USEPA HPV Challenge Program, testing is proposed following OECD Guideline 105 to fulfill the water solubility endpoint.

ENVIRONMENTAL FATE. Values for SAS photodegradation and atmospheric oxidation were calculated based upon representative chemical structures using EPIWIN; no further tested is proposed. Components in SAS do not undergo hydrolysis as they do not contain hydrolysable components. As a result, no further

hydrolysis testing is warranted for SAS. Results from the Level III fugacity modeling of representative structures indicate that releases of SAS to water would remain in water and releases to soil would remain in soil while releases to air would partition primarily to soil. Further fugacity modeling is not warranted for the USEPA HPV Challenge Program. Lastly, SAS has been tested in a Ready Biodegradation test and was not readily biodegradable (3 to 6% in 28 days and 0% in 56 days). No further biodegradability testing is proposed. The weight of evidence in this test plan supports that no further environmental fate testing is necessary to meet HPV SIDS endpoints relating to environmental fate; therefore, no additional testing is proposed for the USEPA HPV Challenge Program.

ACUTE AQUATIC TOXICITY. Acute fish, daphnid, and algal endpoints for SAS are fulfilled with valid studies that were conducted consistent with relevant OECD and USEPA guidelines. No further testing is proposed.

ACUTE MAMMALIAN TOXICITY. Available mammalian toxicity data on SAS (and its structural surrogates that represent the most toxicologically significant SAS constituents) indicate a low order of toxicity. SAS has only been tested for acute toxicity via the oral route, where results are of a similar order of magnitude for both SAS and all of the structural surrogates included in this test plan. Acute dermal and inhalation toxicity results for the various structural surrogates likewise demonstrate a low order of toxicity for this class of materials. No further acute toxicity testing is proposed.

REPEATED DOSE TOXICITY. While multiple repeated dose toxicity studies are available for SAS surrogates encompassing the alkyl aryl, naphthenic, and asphalt functional groups, these data do not entirely address this endpoint for SAS. A 28-day combined, repeated dose, and reproductive/developmental toxicity screening study (OECD Guideline 422) is proposed.

GENETIC TOXICITY. Genotoxicity data exist for all three structural surrogates, Petroleum-derived Sulfonic Acids, Naphthenic Acids, and Asphalts. However, no specific genotoxicity data is available for SAS. CPChem proposes to conduct an AMES Test (OECD 471) to support use of surrogate data presented in this test plan. Based on the evaluation of these data, further genotoxicity tests may be required, ie, *in vivo* micronucleus test (OECD 474).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY. Neither SAS nor any of its structural surrogates have been tested for reproductive and developmental toxicity. To provide definitive data for SAS, testing is proposed following OECD Guideline 422 "Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test".

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Appendix II

DATA QUALITY ASSESSMENT

Available environmental, ecotoxicity, and mammalian toxicity studies were reviewed and assessed for reliability according to standards specified by Klimisch et al., (1997), as recommended by the USEPA (1999a) and the OECD (OECD, 2002). The following reliability classification (Klimisch rating) has been applied to each study assessed:

- *1 = Reliable without Restriction* – Includes studies that comply with USEPA- and/or OECD-accepted testing guidelines and were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented;

- *2 = Reliable with Restriction* – Includes studies that were conducted according to national/international testing guidance and are well documented. May include studies that were conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters that are well documented and scientifically valid but vary slightly from current testing guidance. Also included in this category were physical-chemical property data obtained from reference handbooks, as well as environmental endpoint values obtained from an accepted method of estimation (e.g., USEPA's EPIWIN estimation program);

- *3 = Not Reliable* – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or in which documentation is insufficient; and,

- *4 = Not Assignable* – This designation is used in this dossier for studies that appear scientifically valid but for which insufficient information is available to adequately judge robustness.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this dossier. Those key studies selected for inclusion are considered typical of the endpoint responses observed in other studies of a similar nature and design that were identified during our search of the literature.

Appendix II

LINKS TO SURROGATE TEST PLANS AND ROBUST SUMMARIES

SURROGATE 1:

Alkaryl Sulfonates
Sulfonic Acids, petroleum salts
CAS Number 68783-96-0 (sodium salt)
CAS Number 61789-86-4 (calcium salt)
CAS Number 61790-48-5 (barium salt)
http://www.epa.gov/chemrtk/alklsulf/c13206tc.htm
Sponsor: American Chemistry Council

SURROGATE 2:

Reclaimed Substances Category
Napthenic Acids, Petroleum, crude
CAS Number 64754-89-8
http://www.epa.gov/chemrtk/resbscat/c14906tc.htm
Sponsor: The American Petroleum Institute Petroleum HPV Testing Group

SURROGATE 3:

Asphalt Category
http://www.epa.gov/chemrtk/asphlcat/c14901tc.htm
Sponsor: The American Petroleum Institute Petroleum HPV Testing Group